

AMENDMENT TO THE SPECIFICATION

Please **cancel** the title of the application and replace it with the following new title:

--Reagents and Methods for Diagnosis of Schizophrenia or of a Developmental Defect of the Brain Based on Measurement of Endooligopeptidase A Activity or Expression--

Please amend the specification to include the Sequence Listing attached hereto.

Please amend the paragraph beginning at page 1, line 1 as follows:

~~Process for the determination of the primary structure of the messenger RNA coding for the human recombinant Endooligopeptidase A (*hEOPA*) [AF217798], and the respective protein sequence [AAF24516]; determination of the human EOPA gene and the production of the human recombinant EOPA; process of generating polyclonal anti-EOPA antibodies in mice; standardization and utilization of synthetic substrates to the characterization of the biochemical and proteolytic properties of *hEOPA*; process of identification and production of inhibitors and antibodies displaying inhibitory activity against either the EOPA catalytic activity or the EOPA ability to interact with oligopeptides acting as a "soluble receptor"; methods of identification of this protein in congenital, infectious and degenerative pathologies of the central nervous system, and methods of determination of EOPA's roles in immunological processes; immunochemical and/or enzymatic diagnosis methods to be employed for the prevention, accompanying the evolution of pathologies, prognosis or the treatment of congenital, infectious and/or degenerative diseases of the central nervous system; use of the interaction properties of ligands with the active center of EOPA, acting either as inhibitors of its enzymatic action and/or interfering with its association with other intracellular proteins, which can be useful for the treatment of neurological, psychiatric and degenerative pathologies.~~ Reagents and Methods for Diagnosis of Schizophrenia or of a Developmental Defect of the Brain Based on Measurement of Endooligopeptidase A Activity or Expression

Please amend the paragraph beginning at page 4, line 9 as follows:

The cDNA coding for the human EOPA was isolated from a human brain cortex cDNA library, purchased from Stratagene (La Jolla, USA), after screening by hybridizations employing radioactive-labeled probes derived from a cDNA sequence coding for the rabbit EOPA, identified and described by the authors of the present invention (Hayashi et al., 2000), and deposited at the GenBank databank under the Acc. No. AF015037 (SEQ ID NO: 1, see Figure 2) and AAB99905, for the cDNA and the corresponding protein, respectively.

Please amend the paragraph beginning at page 4, line 11 as follows:

This approximately 2.2 kb long cDNA was completely sequenced, and the sequence was deposited at GenBank under the Acc. No. AF217798 (SEQ ID NO: 2) and AAF24516 (SEQ ID NO: 3), for the cDNA and the protein sequences, respectively.

Please amend the paragraph beginning at page 12, line 4, as follows:

Currently, the peptide of choice used for the determination of the EOPA activity is Abz-GFAPFRQ-EDDnp (SEQ ID NO: 4). This method of characterization of the natural EOPA was applied to the recombinant enzyme, completely reproducing the results obtained with the natural EOPA (Hayashi et al., 2000). This method for enzymatic assay was largely employed to test several peptide substrates with quenched fluorescence, which was used to characterize several tissue oligopeptidases such as the EOPA, TOP and NL (Oliveira et al., 2001).

Please amend the paragraph beginning at page 15, line 1 as follows:

Among the tissues (brain, testes, heart, spleen, liver, lung, skeletal muscle, and kidney) analyzed for the proteolytic activity, we observed that the cytosol of kidney showed the lowest EOPA and neurolysin activity levels. On the other hand, the thimet oligopeptidase (TOP) participates with 32% of the total activity in this tissue, when the substrate Abz-GFAPFRQ-

EDDnp (SEQ ID NO: 4) was used, showing an ubiquitous distribution of this enzyme. In general manner, the enzymatic activity of EOPA and thimet oligopeptidase is homogenously distributed in the cytosol of the most of tissues, with exception for the cytosol of the brain and kidney.

Please amend the paragraph beginning at page 15, line 20 as follows:

In order to better demonstrate the characteristics identified above, which are objects of the present invention, the table above shows the distribution of EOPA, determined by the specific activity of the anti-EOPA antiserum, on the percentage of hydrolysis of the fluorescent substrate Abz-GFAPFRQ-EDDnp (SEQ ID NO: 4) by the cytosolic endooligopeptidases.

Please amend the paragraph beginning at page 15, line 27 as follows:

Additionally it can also be seen in figure 1, that refers to the percentage of endooligopeptidase activities with the substrate Abz-GFAPFRQ-EDDnp (SEQ ID NO: 4).